

What is claimed is:

1. An IRM delivery device adapted for delivery of an IRM compound comprising a microneedle device having at least one microneedle that penetrates a biological barrier by no more than 500  $\mu\text{m}$ , and at least one IRM compound that is a TLR 6, 7, 8, and/or 9 agonist, with the proviso that when the IRM compound is located in a reservoir or coating on the microneedle device along with a vaccine the IRM compound is other than imiquimod or resiquimod.

2. The IRM delivery device of claim 1 wherein the microneedle device comprises a plurality of microneedles.

3. The IRM delivery device of claim 2 wherein the microneedle device comprises at least 5 microneedles.

4. The IRM delivery device of claim 3 wherein the microneedle device comprises at least 100 microneedles.

5. The IRM delivery device of claim 1 wherein the at least one IRM compound is coated onto at least a portion of the microneedle device.

6. The IRM delivery device of claim 1 wherein the microneedle device comprises a reservoir in fluid communication with at least one microneedle, where the reservoir contains the at least one IRM compound.

7. The IRM delivery apparatus of claim 6 further comprising a pump and/or a microprocessor.

8. The IRM delivery device of claim 1 wherein at least one microneedle is hollow.

9. The IRM delivery device of claim 1 wherein at least one microneedle is porous.

10. The IRM delivery device of claim 1 comprising more than one IRM compound.
11. The IRM delivery device of claim 1 further comprising at least one additional drug.
- 5 12. The IRM delivery device of claim 11 wherein the additional drug is a vaccine.
13. The IRM delivery device of claim 11 wherein both the at least one IRM compound and the additional drug are coated onto at least a portion of the microneedle device.
- 10 14. The IRM delivery device of claim 12 wherein the at least one IRM compound is coated onto at least a portion of the microneedle device and wherein the vaccine is not in contact with the IRM delivery device.
- 15 15. The IRM delivery device of claim 12 wherein the vaccine is a DNA vaccine.
16. The IRM delivery device of claim 12 wherein the vaccine is a cell-based vaccine.
17. The IRM delivery device of claim 11 wherein the additional drug is a TNF  
20 receptor agonist.
18. The IRM delivery device of claim 17 wherein the TNF receptor agonist is a CD40 agonist.
- 25 19. The IRM delivery device of claim 11 wherein the additional drug includes both a vaccine and a TNF receptor agonist.
20. The IRM delivery device of claim 12 wherein the at least one IRM compound is physically or chemically linked to a vaccine so as to form a unified pair.
- 30 21. The IRM delivery device of claim 1 wherein the IRM compound is a non-TLR 7 agonist.

22. The IRM delivery device of claim 21 wherein the IRM compound is a TLR 8 agonist.

23. The IRM delivery device of claim 21 wherein the IRM compound is a TLR 9 agonist.

24. The IRM delivery device of claim 1 wherein the IRM compound is a CTL cell activator.

25. The IRM delivery device of claim 1 wherein at least one IRM compound is selected from the group consisting of imidazoquinoline amines including, but not limited to, amide substituted imidazoquinoline amines, sulfonamide substituted imidazoquinoline amines, urea substituted imidazoquinoline amines, aryl ether substituted imidazoquinoline amines, heterocyclic ether substituted imidazoquinoline amines, amido ether substituted imidazoquinoline amines, sulfonamido ether substituted imidazoquinoline amines, urea substituted imidazoquinoline ethers, and thioether substituted imidazoquinoline amines; tetrahydroimidazoquinoline amines including, but not limited to, amide substituted tetrahydroimidazoquinoline amines, sulfonamide substituted tetrahydroimidazoquinoline amines, urea substituted tetrahydroimidazoquinoline amines, aryl ether substituted tetrahydroimidazoquinoline amines, heterocyclic ether substituted tetrahydroimidazoquinoline amines, amido ether substituted tetrahydroimidazoquinoline amines, sulfonamido ether substituted tetrahydroimidazoquinoline amines, urea substituted tetrahydroimidazoquinoline ethers, and thioether substituted tetrahydroimidazoquinoline amines; imidazopyridine amines including, but not limited to, amide substituted imidazopyridines, sulfonamido substituted imidazopyridines, and urea substituted imidazopyridines; 1,2-bridged imidazoquinoline amines; 6,7-fused cycloalkylimidazopyridine amines; imidazonaphthyridine amines; tetrahydroimidazonaphthyridine amines; oxazoloquinoline amines; thiazoloquinoline amines; oxazolopyridine amines; thiazolopyridine amines; oxazolonaphthyridine amines; thiazolonaphthyridine amines; and pharmaceutically acceptable salts thereof; and combinations thereof.

26. The IRM delivery device of claim 1 wherein the IRM is selected from the group consisting of amide substituted imidazoquinoline amines, sulfonamide substituted imidazoquinoline amines, urea substituted imidazoquinoline amines, aryl ether substituted imidazoquinoline amines, heterocyclic ether substituted imidazoquinoline amines, amido ether substituted imidazoquinoline amines, sulfonamido ether substituted imidazoquinoline amines, urea substituted imidazoquinoline ethers, and thioether substituted imidazoquinoline amines; tetrahydroimidazoquinoline amines including, but not limited to, amide substituted tetrahydroimidazoquinoline amines, sulfonamide substituted tetrahydroimidazoquinoline amines, urea substituted tetrahydroimidazoquinoline amines, aryl ether substituted tetrahydroimidazoquinoline amines, heterocyclic ether substituted tetrahydroimidazoquinoline amines, amido ether substituted tetrahydroimidazoquinoline amines, sulfonamido ether substituted tetrahydroimidazoquinoline amines, urea substituted tetrahydroimidazoquinoline ethers, and thioether substituted tetrahydroimidazoquinoline amines; imidazopyridine amines including, but not limited to, amide substituted imidazopyridines, sulfonamido substituted imidazopyridines, and urea substituted imidazopyridines; 1,2-bridged imidazoquinoline amines; 6,7-fused cycloalkylimidazopyridine amines; imidazonaphthyridine amines; tetrahydroimidazonaphthyridine amines; oxazoloquinoline amines; thiazoloquinoline amines; oxazolopyridine amines; thiazolopyridine amines; oxazolonaphthyridine amines; thiazolonaphthyridine amines; pharmaceutically acceptable salts thereof; and combinations thereof.

27. The IRM delivery device of claim 1 wherein at least one IRM compound is selected from the group consisting of purines, imidazoquinoline amides, benzimidazoles, 1H-imidazopyridines, adenines, and derivatives thereof.

28. The IRM delivery device of claim 1 wherein at least one IRM compound comprises a 2-aminopyridine fused to a five-membered nitrogen-containing heterocyclic ring.

29. The IRM delivery device of claim 1 wherein at least one IRM compound comprises a 4-aminopyrimidine fused to a five-membered nitrogen-containing heterocyclic ring.

5 30. The IRM delivery device of claim 1 wherein at least one IRM compound comprises a CpG compound or derivative thereof.

31. The IRM delivery device of claim 1 wherein at least one IRM compound is 2-propyl[1,3]thiazolo[4,5-*c*]quinolin-4-amine, or pharmaceutically acceptable salt thereof.

10 32. The IRM delivery device of claim 1 wherein at least one IRM compound is 4-amino- $\alpha,\alpha$ -dimethyl-1*H*-imidazo[4,5-*c*]quinoline-1-ethanol, or pharmaceutically acceptable salt thereof.

15 33. An IRM delivery device adapted for delivery of an IRM compound comprising a microneedle device having at least one microneedle that penetrates a biological barrier by no more than 500  $\mu\text{m}$ , and at least one IRM compound that is a TLR 6, 7, 8, and/or 9 agonist, with the proviso that a vaccine is not in contact with the microneedle device prior to administration of the IRM compound.

20 34. An IRM delivery device adapted for delivery of an IRM compound comprising a microneedle device having at least one microneedle that penetrates a biological barrier by no more than 500  $\mu\text{m}$ , and at least one IRM compound that is a TLR 6, 8, and/or 9 agonist, but not a TLR 7 agonist.

25 35. A method for the delivery of an IRM compound into or across a biological barrier comprising:

contacting a biological barrier with a microneedle device comprising at least one microneedle that penetrates the barrier by no more than 500  $\mu\text{m}$ ;

30 administering at least one IRM compound that is a TLR 6, 7, 8, and/or 9 agonist into or across the biological barrier; and

optionally administering a vaccine;

with the proviso that when the IRM compound is located in a reservoir or coating on the microneedle device along with the vaccine, the IRM compound is other than imiquimod or resiquimod.

5      36.      The method of claim 35 wherein the biological barrier is the skin and the at least one IRM compound is delivered intracutaneously.

37.      The method of claim 36 wherein contacting the skin with a microneedle device occurs prior to contacting the skin with at least one IRM compound.

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38.      The method of claim 36 wherein contacting the skin with at least one IRM compound comprises applying the at least one IRM compound topically to the skin.

15      39.      The method of claim 38 wherein the at least one IRM compound is contained in a solution, ointment, gel, foam, or emulsion.

40.      The method of claim 36 wherein contacting the skin with at least one IRM compound occurs prior to contacting the skin with a microneedle device.

20      41.      The method of claim 40 wherein contacting the skin with at least one IRM compound comprises applying the at least one IRM compound topically to the skin.

42.      The method of claim 41 wherein the at least one IRM compound is contained in a solution, ointment, gel, foam, or emulsion.

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43.      The method of claim 36 wherein contacting the skin with a microneedle device occurs coincident with contacting the skin with at least one IRM compound.

30      44.      The method of claim 43 wherein the at least one IRM compound is coated on at least a portion of the microneedle device.

45. The method of claim 36 further comprising the intracutaneous administration of a vaccine.

46. The method of claim 35 wherein at least one IRM compound is a small molecule immune response modifier.

47. The method of claim 35 wherein at least one IRM compound is selected from the group consisting of imidazoquinoline amines including, but not limited to, amide substituted imidazoquinoline amines, sulfonamide substituted imidazoquinoline amines, urea substituted imidazoquinoline amines, aryl ether substituted imidazoquinoline amines, heterocyclic ether substituted imidazoquinoline amines, amido ether substituted imidazoquinoline amines, sulfonamido ether substituted imidazoquinoline amines, urea substituted imidazoquinoline ethers, and thioether substituted imidazoquinoline amines; tetrahydroimidazoquinoline amines including, but not limited to, amide substituted tetrahydroimidazoquinoline amines, sulfonamide substituted tetrahydroimidazoquinoline amines, urea substituted tetrahydroimidazoquinoline amines, aryl ether substituted tetrahydroimidazoquinoline amines, heterocyclic ether substituted tetrahydroimidazoquinoline amines, amido ether substituted tetrahydroimidazoquinoline amines, sulfonamido ether substituted tetrahydroimidazoquinoline amines, urea substituted tetrahydroimidazoquinoline ethers, and thioether substituted tetrahydroimidazoquinoline amines; imidazopyridine amines including, but not limited to, amide substituted imidazopyridines, sulfonamido substituted imidazopyridines, and urea substituted imidazopyridines; 1,2-bridged imidazoquinoline amines; 6,7-fused cycloalkylimidazopyridine amines; imidazonaphthyridine amines; tetrahydroimidazonaphthyridine amines; oxazoloquinoline amines; thiazoloquinoline amines; oxazolopyridine amines; thiazolopyridine amines; oxazonaphthyridine amines; thiazolonaphthyridine amines; a pharmaceutically acceptable salt thereof; and combinations thereof.

48. The method of claim 47 wherein the IRM is selected from the group consisting of amide substituted imidazoquinoline amines, sulfonamide substituted imidazoquinoline amines, urea substituted imidazoquinoline amines, aryl ether substituted imidazoquinoline

amines, heterocyclic ether substituted imidazoquinoline amines, amido ether substituted imidazoquinoline amines, sulfonamido ether substituted imidazoquinoline amines, urea substituted imidazoquinoline ethers, and thioether substituted imidazoquinoline amines; tetrahydroimidazoquinoline amines including, but not limited to, amide substituted tetrahydroimidazoquinoline amines, sulfonamide substituted tetrahydroimidazoquinoline amines, urea substituted tetrahydroimidazoquinoline amines, aryl ether substituted tetrahydroimidazoquinoline amines, heterocyclic ether substituted tetrahydroimidazoquinoline amines, amido ether substituted tetrahydroimidazoquinoline amines, sulfonamido ether substituted tetrahydroimidazoquinoline amines, urea substituted tetrahydroimidazoquinoline ethers, and thioether substituted tetrahydroimidazoquinoline amines; imidazopyridine amines including, but not limited to, amide substituted imidazopyridines, sulfonamido substituted imidazopyridines, and urea substituted imidazopyridines; 1,2-bridged imidazoquinoline amines; 6,7-fused cycloalkylimidazopyridine amines; imidazonaphthyridine amines; tetrahydroimidazonaphthyridine amines; oxazoloquinoline amines; thiazoloquinoline amines; oxazolopyridine amines; thiazolopyridine amines; oxazolonaphthyridine amines; thiazolonaphthyridine amines; pharmaceutically acceptable salts thereof; and combinations thereof.

49. The method of claim 35 wherein at least one IRM compound is selected from the group consisting of purines, imidazoquinoline amides, benzimidazoles, 1H-imidazopyridines, adenines, and derivatives thereof.

50. The method of claim 35 wherein at least one IRM compound comprises a 2-aminopyridine fused to a five-membered nitrogen-containing heterocyclic ring.

51. The method of claim 35 wherein at least one IRM compound comprises a 4-aminopyrimidine fused to a five-membered nitrogen-containing heterocyclic ring.

52. A method for the delivery of an IRM compound into or across a biological barrier comprising:



contacting a biological barrier with a microneedle device comprising at least one microneedle that penetrates the barrier by no more than 500  $\mu\text{m}$ ;

administering at least one IRM compound that is a TLR 6, 7, 8, and/or 9 agonist into or across the biological barrier; and

5 optionally administering a vaccine;

with the proviso that the vaccine is not in contact with the microneedle device prior to administration of the IRM compound.

10 53. A method for the delivery of an IRM compound into or across a biological barrier comprising:

contacting a biological barrier with a microneedle device comprising at least one microneedle that penetrates the barrier by no more than 500  $\mu\text{m}$ ; and

administering at least one IRM compound that is a TLR 6, 8, and/or 9 agonist, but not a TLR 7 agonist, into or across the biological barrier.

15 54. A method of treating a lesion on the skin or mucosa comprising application of a microneedle device to the lesion in conjunction with the application of at least one IRM compound.

20 55. The method of claim 54 wherein the lesion is a neoplastic condition.

56. The method of claim 55 wherein the lesion is associated with melanoma.

25 57. The method of claim 55 wherein the lesion is associated with basal cell carcinoma, actinic keratosis, or squamous cell carcinoma.

58. The method of claim 54 wherein the lesion is associated with a viral infection.

59. The method of claim 58 wherein the lesion is a wart.

30 60. A kit comprising a microneedle device and one or more IRM compounds separate from the microneedle device.